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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/886,171	06/20/2001	David Zarling	A-66914-2/RFT/NBC	8414

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RICHARD F. TRECARTIN, ESQ.
FLEHR HOHBACH TEST ALBRITTON & HERBERT LLP
Suite 3400
Four Embarcadero Center
San Francisco, CA 94111-4187

EXAMINER

LAMBERTSON, DAVID A

ART UNIT PAPER NUMBER

1636

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/886,171	Applicant(s) ZARLING ET AL.	
	Examiner David A. Lambertson	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 7, 8 and 10-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 3, 4, 16, 17, 26 and 29 is/are allowed.
- 6) ☒ Claim(s) 1, 7, 10-13 and 18-24 is/are rejected.
- 7) ☒ Claim(s) 2, 8, 14, 25, 27 and 28 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed August 5, 2003.

Amendments were made to the claims. Specifically, claims 5, 6 and 9 were cancelled

Claims 1-5, 7, 8 and 10-29 are pending and under consideration in the instant application.

It is noted that applicant has indicated in their remarks that claim 27 has been cancelled; however, the claim is still iterated in the claim amendments, and has been treated as pending because it is unclear if the claim has indeed been cancelled (see also the Objections to the Claims). Any rejection of record in the previous Office Action, mailed October 1, 2002, that is not addressed in this action has been withdrawn.

Response to Arguments

Applicant's arguments with respect to claims 1-29 have been considered but are moot in view of the new ground(s) of rejection. However, it is important to note that in Applicant's traversal of the rejection of claims 1, 2, 5-14 and 16-29 as anticipated under 35 USC 102(e) by *Pati et al.* (US 5,948,653), it is argued that *Pati et al.* specifically does not teach a repeating step. It is agreed that this "repeating step" is absent from the teachings, although this point is addressed in the following rejections.

Specification

The disclosure is objected to because of the following informalities: the specification contains numerous US Patent Application numbers that require an update in status as either

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abandoned or by indication of the US Patent number (see for example page 3, lines 5-7, and others).

Appropriate correction is required.

Information Disclosure Statement

It appears that Applicant's information disclosure statement "crossed over" with the previous Office Action, and was not considered on the record. As such, the information disclosure statement filed September 16, 2002 has now been considered, and a signed and initialed copy of the form PTO-1449 is attached to this Office Action. The Office apologizes for the delay in the consideration of the IDS.

Claim Objections

Claim 27 is objected to because of the following informalities: Claim 27 depends from a claim that has been cancelled. It appears that it was Applicant's intent to cancel the claim, although the claim is still present in the claims as amended. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the claim lacks a period at the end of the claim, thus it is unclear if

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the claim has additional limitations. It would be remedial to place a period at the end of the claim. **This is a new rejection necessitated by amendment.**

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 7, 10-13, 15 and 18-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pati et al. (US 5,948,653; see entire document as cited in the previous Office Action; henceforth, Pati) in view of delCardayre et al. (US 6,326,204; see entire document; henceforth delCardayre). **This is a new rejection necessitated by amendment.**

Pati teaches all of the elements of the claim as set forth in the previous Office Action, except for the “repeating step” where the recombination event is reiterated. Briefly, Pati teaches methods of targeting an exogenous polynucleotide (henceforth targeting polynucleotide) to a target sequence, using a complementary region between the targeting polynucleotide and the target sequence, whereby a homologous recombination event occurs thereby resulting in a modification of the target sequence (see for example column 6, lines 46-52). The targeting event is performed by first selecting the target sequence and then contacting the target sequence with a recombinase and two single stranded targeting polynucleotides. The single stranded polynucleotides are each substantially complementary to each other and comprise “homology clamp” that is substantially complementary to the target sequence (see for example column 19,

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lines 19-30). The method is used to generate pools or libraries of variant nucleic acid sequences (see for example column 34, lines 23-26) by using targeting polynucleotides that comprise “mismatches” that are used to introduce the variants into the target sequence (see for example column 34, lines 50-64). In a particular embodiment, these variants are generated in specific protein domains, which is the definition of “domain specific gene evolution” (see for example column 35, lines 13-35). The method described by Pati contemplates that the target sequence can be present in both an endogenous sequence such as a chromosome (see for example column 7, lines 3-6), or in an extrachromosomal sequence (see for example column 29, lines 28-63). Furthermore, the method contemplates making the modifications in either prokaryotic or eukaryotic cells (see for example column 9, lines 21-31 and column 6, lines 54-61), using either prokaryotic, eukaryotic or endogenous recombinase proteins to perform the recombination event (see for example column 26, lines 31-35). In some embodiments, the targeting polynucleotides are first coated with the recombinase (see for example column 28, lines 25-31). Finally, Pati contemplates using a targeting polynucleotide containing a chemical substituent (see for example column 27, lines 40-53).

As stated above, Pati does not teach repeating the contacting/recombination step.

DelCardayre teaches a method for artificially evolving cells to acquire a new property, where the method comprises successive cycles of recombination events to maximize molecular diversity, using a library of diverse nucleic acid molecules (see for example column 9, lines 23-38 and column 10, lines 35-45). Although delCardayre contemplates that this method can be used for the diversification of genes without the need to focus solely on those genes that have been characterized, delCardayre also teaches that the method can be used in a more focused

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manner. Specifically, delCardayre recognizes that any individual, specific gene (i.e., a target sequence) can be "evolved" through their described method, which requires reiterative recombination events with a library of nucleic acid sequences (i.e., targeting polynucleotides) (see for example column 16, lines 24-47). Thus, delCardayre provides a general teaching that reiterative cycles of recombination can be utilized to evolve a gene.

The ordinary skilled artisan would recognize that the teachings of both delCardayre and Pati involve the forced evolution of genes using a process of recombination between targeting polynucleotides and a target sequence, therefore it would be obvious to combine the teachings of delCardayre and Pati because they both use the same general techniques in order to accomplish the same goal. The ordinary skilled artisan would have been motivated to combine the teachings in order to achieve the most advantageous level of evolution/molecular diversity of the target sequence, which is suggested by the multiple rounds of recombination practiced in the teachings of delCardayre. Absent evidence to the contrary, and in light of the interrelated nature of the teachings of delCardayre and Pati, the ordinary skilled artisan would have had a reasonable expectation of success when practicing the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 10 and 15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2 and 9 of U.S. Patent No. 6,074,853 (henceforth the '853 Patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '853 patent encompass the scope of the instant claims, and it is recited in the specification of the '853 patent that the instant claims are a preferred embodiment of the claimed invention. Although the standard of Double Patenting is generally reserved for a comparison of the claims, in instances where generic claims are issued and the specification teaches a specific or preferred embodiment of the claims that would be obvious to the skilled artisan, it is proper to use the specification to define the embodiments of the claims. In this instance, the instant claims are a preferred species within the genus claims of the '853 patent, and the skilled artisan would clearly understand from the disclosure in the '853 patent (see for example column 36, lines 18-51) that the instantly claimed methods of domain specific gene evolution (the equivalent of a pool of variant nucleic acids of a pre-selected target sequence) were a specific embodiment of the invention claimed in the '853 patent. Since there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent, and the skilled artisan would understand that the instant claims were a preferred embodiment of the issued claims, the instant claims are subject to the judicially created doctrine of obviousness-type double patenting.

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Allowable Subject Matter

Claims 3, 4, 16, 17, 26 and 29 are allowed.

Claims 2, 8, 14, 25 and 28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson, Ph.D
AU 1636


JAMES KETTER
PRIMARY EXAMINER